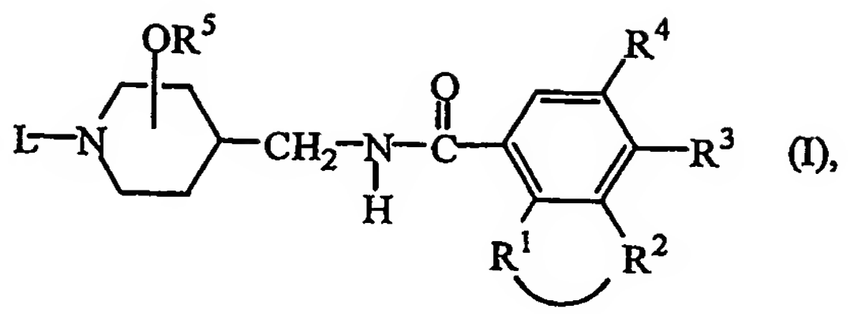
Claims

1. A compound of formula (I)



(I),

a stereochemically isomeric form thereof, an *N*-oxide form thereof, or a pharmaceutically acceptable acid or base addition salt thereof, wherein

$-R^1-R^2-$ is a bivalent radical of formula

$-O-CH_2-O-$ (a-1),

$-O-CH_2-CH_2-$ (a-2),

$-O-CH_2-CH_2-O-$ (a-3),

$-O-CH_2-CH_2-CH_2-$ (a-4),

$-O-CH_2-CH_2-CH_2-O-$ (a-5),

$-O-CH_2-CH_2-CH_2-CH_2-$ (a-6),

$-O-CH_2-CH_2-CH_2-CH_2-O-$ (a-7),

$-O-CH_2-CH_2-CH_2-CH_2-CH_2-$ (a-8),

wherein in said bivalent radicals optionally one or two hydrogen atoms on the same or a different carbon atom may be replaced by C_{1-6}alkyl or hydroxy,

R^3 is C_{1-6}alkyl, C_{1-6}alkyloxy, or halo;

R^4 is hydrogen or halo;

provided that when R^3 and R^4 are both halo, then the bivalent radical $-R^1-R^2-$ is of formula (a-5);

R^5 is hydrogen or C_{1-6}alkyl, and the $-OR^5$ radical is situated at the 3- or 4-position of the piperidine moiety;

L is hydrogen, or L is a radical of formula

$-Alk-R^6$ (b-1),

$-Alk-X-R^7$ (b-2),

$-Alk-Y-C(=O)-R^9$ (b-3), or

$-Alk-Z-C(=O)-NR^{11}R^{12}$ (b-4),

wherein each Alk is C_{1-12}alkanediyl; and

R^6 is hydrogen; hydroxy; cyano; C_{3-6}cycloalkyl; C_{1-6}alkylsulfonylamino; aryl or Het;

R^7 is C_{1-6}alkyl; C_{1-6}alkyl substituted with hydroxy; C_{3-6}cycloalkyl; aryl or Het;

X is O, S, SO_2 or NR^8; said R^8 being hydrogen or C_{1-6}alkyl;

R^9 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, hydroxy or aryl;

Y is a direct bond, or NR^{10} wherein R^{10} is hydrogen or C_{1-6}alkyl;

Z is a direct bond, O, S, or NR^{10} wherein R^{10} is hydrogen or C_{1-6}alkyl;

R^{11} and R^{12} each independently are hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, or R^{11} and R^{12} combined with the nitrogen atom bearing R^{11} and R^{12} may form a pyrrolidinyl, piperidinyl, piperazinyl or 4-morpholinyl ring both being optionally substituted with C_{1-6}alkyl;

aryl represents unsubstituted phenyl or phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, hydroxy, C_{1-6}alkyl, C_{1-6}alkyloxy, C_{1-6}alkylcarbonyl, nitro, trifluoromethyl, amino, aminocarbonyl, and aminosulfonyl; and

Het is furanyl; furanyl substituted with C_{1-6}alkyl or halo;
tetrahydrofuranyl; tetrahydrofuranyl substituted with C_{1-6}alkyl;
dioxolanyl; dioxolanyl substituted with C_{1-6}alkyl;
dioxanyl; dioxanyl substituted with C_{1-6}alkyl;
tetrahydropyranyl; tetrahydropyranyl substituted with C_{1-6}alkyl;
2,3-dihydro-2-oxo-1H-imidazolyl; 2,3-dihydro-2-oxo-1H-imidazolyl substituted with one or two substituents each independently selected from halo, or C_{1-6}alkyl;
pyrrolidinyl; pyrrolidinyl substituted with one or two substituents each independently selected from halo, hydroxy, or C_{1-6}alkyl;
pyridinyl; pyridinyl substituted with one or two substituents each independently selected from halo, hydroxy, C_{1-6}alkyl;
pyrimidinyl; pyrimidinyl substituted with one or two substituents each independently selected from halo, hydroxy, or C_{1-6}alkyl;
pyridazinyl; pyridazinyl substituted with one or two substituents each independently selected from hydroxy, C_{1-6}alkyloxy, C_{1-6}alkyl or halo;
pyrazinyl; pyrazinyl substituted with one ore two substituents each independently selected from hydroxy, C_{1-6}alkyloxy, C_{1-6}alkyl or halo.

2. A compound as claimed in claim 1 wherein the $-OR^5$ radical is situated at the 3-position of the piperidine moiety having the trans configuration.

3. A compound as claimed in claim 2 wherein the absolute configuration of said piperidine moiety is (3S, 4S).

4. A compound as claimed in any of claims 1 to 3 wherein $-R^1-R^2-$ is a radical of formula (a-5), R^3 is chloro and R^4 is chloro.

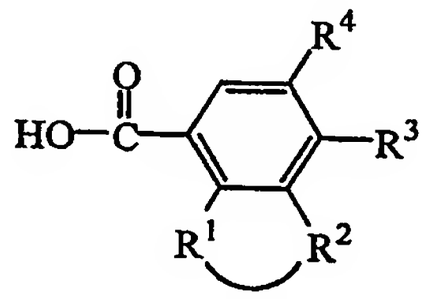
5. A compound as claimed in any of claims 1 to 3 wherein $-R^1-R^2-$ is a radical of formula (a-5), R^3 is chloro and R^4 is bromo.

6. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically active amount of a compound according to any of claims 1 to 5.

7. A process for preparing a pharmaceutical composition according to claim 6 wherein a therapeutically active amount of a compound according to any of claims 1 to 5 is intimately mixed with a pharmaceutically acceptable carrier.

8. A compound according to any of claims 1 to 5 for use as a medicine.

9. A compound of formula (III) .



(III)

wherein

$-R^1-R^2-$ is a bivalent radical of formula

$$-O-CH_2-CH_2-CH_2-O- \qquad (a\text{-}5),$$

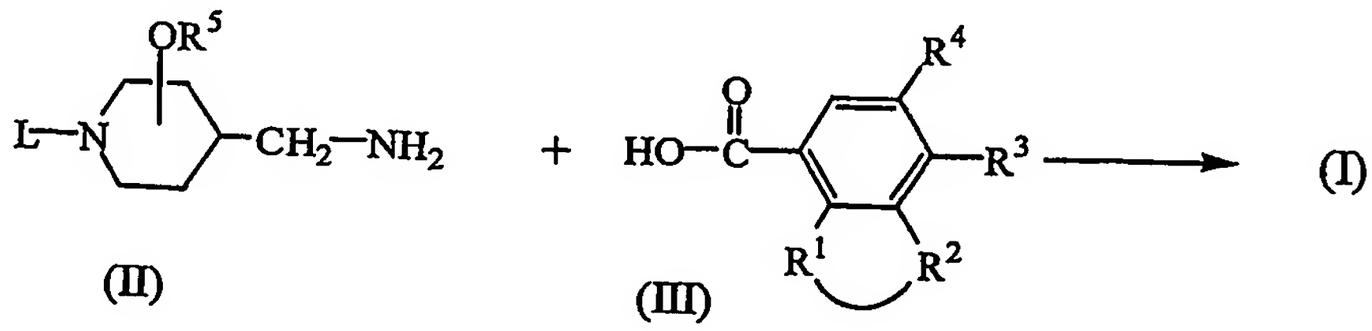
wherein in said bivalent radicals optionally one or two hydrogen atoms on the same or a different carbon atom may be replaced by C_{1-6}alkyl or hydroxy;

R^3 is C_{1-6}alkyl, C_{1-6}alkyloxy, or halo; and

R^4 is hydrogen or halo.

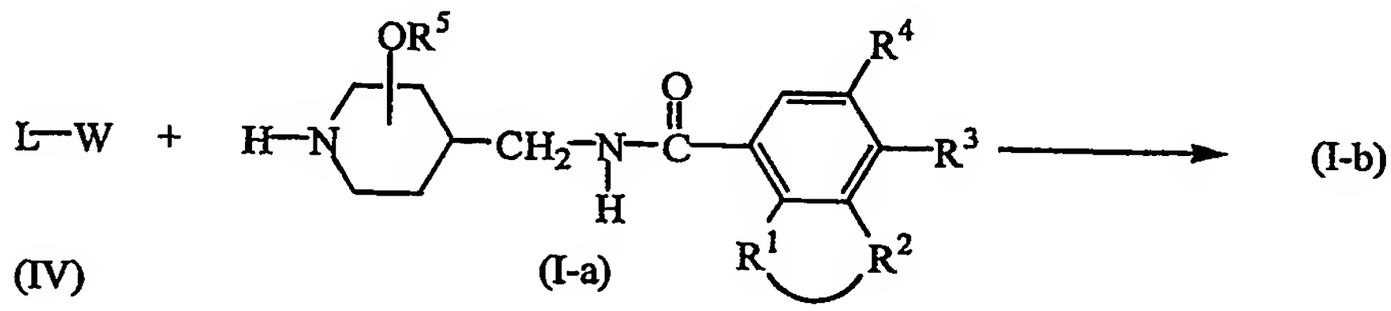
10. A process for preparing a compound of formula (I) wherein

a) an intermediate of formula (II) is reacted with an carboxylic acid derivative of formula (III) or a reactive functional derivative thereof;



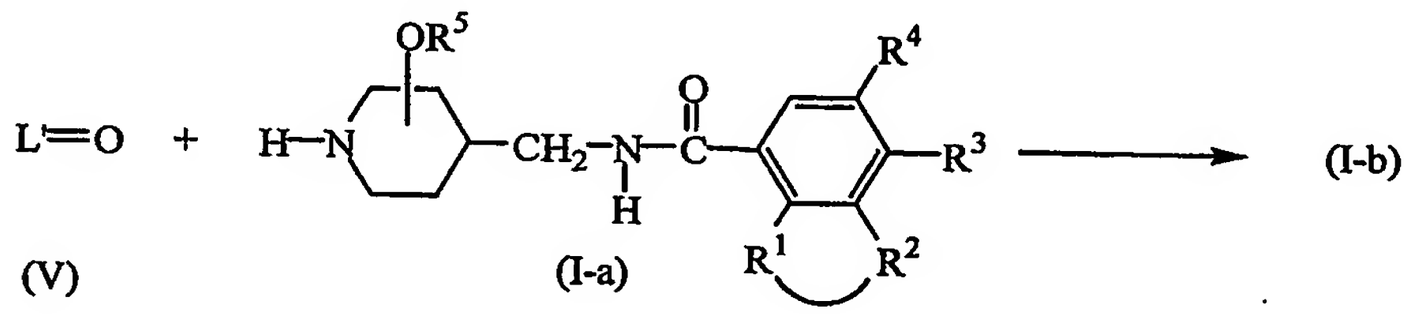
(II) (III) (I)

b) an intermediate of formula (IV) is *N*-alkylated with a compound of formula (I-a), defined as a compound of formula (I) wherein L represents hydrogen, in a reaction-inert solvent and, optionally in the presence of a suitable base, thereby yielding compounds of formula (I-b), defined as compounds of formula (I) wherein L is other than hydrogen;



(IV) (I-a) (I-b)

c) an appropriate ketone or aldehyde intermediate of formula L'=O (V), said L'=O being a compound of formula L-H, wherein two geminal hydrogen atoms in the C_{1-12}alkanediyl moiety are replaced by =O, is reacted with a compound of formula (I-a), thereby yielding compounds of formula (I-b);



(V) (I-a) (I-b)

wherein in the above reaction schemes the radicals $-R^1-R^2-$, R^3, R^4 and R^5 are as defined in claim 1 and W is an appropriate leaving group;

d) or, compounds of formula (I) are converted into each other following art-known transformation reactions; or if desired; a compound of formula (I) is converted into a pharmaceutically acceptable acid addition salt, or conversely, an acid addition salt of a compound of formula (I) is converted into a free base form with alkali; and, if desired, preparing stereochemically isomeric forms thereof.